# Are Antibiotics a Viable Alternative to Surgery for Acute Appendicitis?

Michael Gottlieb, MD, Department of Emergency Medicine, Cook County Hospital, Chicago, IL
Benton Hunter, MD, Department of Emergency Medicine, Indiana University School of Medicine, Indianapolis, IN

**Take Home Message:**

Antibiotics alone may be a reasonable option for non-perforated acute appendicitis as an alternative to surgery, but a significant number of antibiotic treated patients may develop recurrent appendicitis requiring appendectomy by one year.

**Methods:**

**Data Sources:**

The authors updated a 2011 Cochrane review. MEDLINE, Embase, and CENTRAL were searched from January 1, 2011 through December 2015. Pubmed was searched for in-process citations. Clinical trial registries (i.e. ClinicalTrials.gov, ICTRP) and references from previous reviews were searched, as well.

**Study Selection:**

Randomized studies comparing antibiotic treatment versus appendectomy in patients with suspected acute non-perforated appendicitis were included. Studies at very high risk of bias were excluded. Quasi-randomized studies were eligible for inclusion in sensitivity analysis.

**Data Extraction and Synthesis:**

The authors worked in teams of 2 using pilot tested forms to extract data independently, with disagreements adjudicated by a 3rd reviewer. Patient characteristics, antibiotic

This is the author's manuscript of the article published in final edited form as:
Gottlieb, M., & Hunter, B. (2016). Are Antibiotics a Feasible Alternative to Surgery for Acute Appendicitis? Annals of Emergency Medicine. https://doi.org/10.1016/j.annemergmed.2016.04.019

regimens, surgical techniques, need for subsequent surgery, and complications were extracted. Authors were contacted to check data for accuracy and provide additional data when needed. Risk of bias was assessed using 4 criteria: random sequence generation, allocation concealment, blinding, and data completeness. Pooled estimates of risk differences were calculated by a random-effects meta-analysis, and heterogeneity was reported using the $I^2$ statistic. Planned subgroup analyses included those with CT confirmation of non-perforated appendicitis and those studies at low risk of bias.

**Results:**

**Summary outcomes of patients randomized to antibiotics or appendectomy**

| | Antibiotics | Appendectomy | Difference (95% CI) |
|---|---|---|---|
| Recurrence of appendicitis 1 year | 22.4% | 0% | 22.4% (15.6% to 30.4%) |
| Major Complications | 4.9% | 8.4% | -2.5% (-6.6% to +1.1%) |
| Major Complications (Only low ROB studies) | 3.0% | 5.4% | -2.4% (-5.8% to +1.0%) |
| Minor Complications | 2.2% | 12.5% | -7.2% (-18.1% to +3.8%) |
| Minor Complications (Only low ROB studies) | 1.8% | 16.5% | -9.0% (-22.8% to +4.8%) |

ROB = Risk of Bias; CI = Confidence Intervals

Of 685 potentially relevant reports, 5 randomized trials were included in the meta-analysis, and one quasi-randomized study was added to the sensitivity analysis. Two randomized trials were excluded for high risk of bias, one for plagiarism and another for post-randomization exclusions. Of note, no patients, healthcare providers, or outcome assessors were blinded in any study. Lost to follow-up rates ranged from 7% to 22% at one year. Two of the included trials required the diagnosis of appendicitis to be

confirmed by CT scan. Two studies were deemed high risk of bias, and 3 were deemed low risk of bias.

Of patients who initially received antibiotic treatment, 8.5% underwent appendectomy by 30 days, and 22.4% had recurrence of appendicitis at one year. Among those treated with antibiotics who developed recurrent appendicitis, the average time to recurrence ranged from 3.4 to 7.0 months; these results were based on high quality evidence. The appendectomy group had a slightly shorter hospital stay (0.4 days), while the antibiotics group demonstrated trends in decreased major and minor complications and decreased length of sick leave, though none of these outcomes reached statistical significance (Table). Almost all major complications in both groups consisted of appendiceal perforation. Comparisons of complication rates were based on low to very low quality evidence; none of the pre-specified subgroup analyses or sensitivity analyses explained differences in the rate of complications.

**Commentary**:

Acute appendicitis is one of the most common indications for emergency abdominal surgery, with an average of 250,000 appendectomies being performed every year in the United States alone (Addiss 1990). Although the mortality rate has significantly decreased, studies have demonstrated an average complication rate of 4-12% (Masoomi 2011 #1, Masoomi 2011 #2).

Since the 1800s, the treatment of choice for appendicitis has been surgical removal of the appendix (Fitz 1886). However, in 1956, Dr. Eric Coldrey challenged this view describing a series of 137 patients with acute appendicitis for greater than 24 hours who were treated with antibiotics rather than surgery (Coldrey 1956). Since then, several randomized trials have compared surgery against antibiotics alone, prompting this systematic review.

In the included trials, antibiotics alone as initial therapy resulted in a 92% decrease in the number of patients receiving surgery within the first month, but a 23% increase in the incidence of recurrent appendicitis within one year. This provides valuable information to help patients make informed choices regarding surgery versus antibiotics alone. Patients who are averse to surgery might elect to use antibiotics, while patients who fear the risk of recurrence might opt for surgery.

It is important to note that 7 to 22% of patients were lost to follow-up in the included studies, which could have influenced the results. Additionally, the patients, healthcare providers, and assessors were not blinded, which may have introduced a measurement bias or issues related to co-intervention. Furthermore, only 22.6% of appendectomies were performed laparoscopically, with the remainder being open appendectomies. This may limit generalizability to current practice, as most appendectomies are now performed laparoscopically (Masoomi 2011 #1). A recent systematic review identified a decreased rates of wound infection and bowel obstruction with the laparoscopic approach (Sauerland 2010), so surgical complications may be over-estimated in the included trials.

Unfortunately, there was no assessment of pain or quality of life between the 2 treatment options. Additionally, trial authors did not report on complications associated with antibiotics (eg, diarrhea, allergic reactions). The medical community must also consider the potential for antibiotic resistance with increased utilization of the antibiotic approach. Finally, it is important to emphasize that this only applies to clinically stable patients without appendiceal perforation and that most studies admitted patients to the hospital for 2-3 days of intravenous antibiotics.

Future studies should assess long term outcomes, effect on healthcare costs, and whether patients could be discharged with oral antibiotics sooner than 2-3 days.

**Editor's Note:**

This is a clinical synopsis, a regular feature of the *Annals'* Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is: **Sallinen V, Akl EA, You JJ, et al. Meta-analysis of antibiotics versus appendicectomy for non-perforated acute appendicitis. Br J Surg. 2016 Mar 17. doi: 10.1002/bjs.10147. [Epub ahead of print]**

**References**


1. Addiss DG, Shaffer N, Fowler BS, et al. The epidemiology of appendicitis and appendectomy in the United States. Am J Epidemiol. 1990 Nov;132(5):910-25.
2. Masoomi H, Mills S, Dolich MO, et al. Comparison of outcomes of laparoscopic versus open appendectomy in adults: data from the Nationwide Inpatient Sample (NIS), 2006-2008. J Gastrointest Surg. 2011 Dec;15(12):2226-31.
3. Masoomi H, Mills S, Dolich MO, et al. Comparison of laparoscopic versus open appendectomy for acute nonperforated and perforated appendicitis in the obese population. Am J Surg. 2011 Dec;202(6):733-8; discussion 738-9.

4. Fitz RH. Perforating inflammation of the vermiform appendix: with special reference to its early diagnosis and treatment. Am J Med Sci. 1886;92:321-46.
5. Coldrey E. Treatment of Acute Appendicitis. Br Med J. 1956 Dec 22;2(5007):1458-61.
6. Sauerland S, Jaschinski T, Neugebauer EA. Laparoscopic versus open surgery for suspected appendicitis. Cochrane Database Syst Rev. 2010 Oct 6;(10):CD001546.